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Synthesis and Antimicrobial Activity of Some New 2-(3′-Phenoxy Phenyl)-3-Aryl-5-Methyl-4-Thiazolidinones

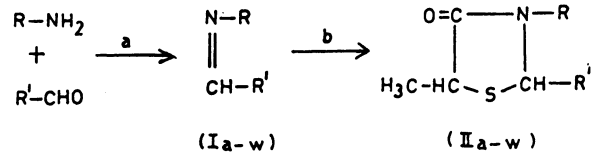
ANJANI SOLANKEE*, JAYESH PATEL, KISHOR KAPADIA,
INDRAJIT THAKOR and KETKI UPADHYAY
Department of Chemistry, B.K.M. Science College
Valsad-396 001, India

2-(3′-Phenoxy phenyl)-3-aryl-5-methyl-4-thiazolidinones (**IIa–w**) have been synthesized by the cyclocondensation of thiolactic acid with Schiff bases (**Ia–w**) which in turn were prepared by the action of *m*-phenoxy benzaldehyde with aryl amines. The structures of the synthesized compounds have been confirmed by elemental analysis, IR and ^{1}H NMR spectral data. All the products were evaluated for their *in vitro* growth inhibitory activity against several microbes like *Staphylococcus aureus, Escherichia coli, Bacillus subtilis, Serratia marcescens, Proteus vulgaris* and *Pseudomonas aeruginosa.*

Key words: Synthesis, Antimicrobial activity, Thiazolidinones.

INTRODUCTION

4-Thiazolidinones play a vital role owing to their wide range of biological activities[1–3]. Some thiazolidinones were found active against *Mycobacterium tuberculosis*[4,5]. Compounds containing thiazolidine ring exhibit variety of biological activities such as antimicrobial[6], insecticidal[7,8], parasiticidal and pharmacological properties. The chemistry of 4-thiazolidinone ring system was reviewed in depth[9]. 4-Thiazolidinones are synthesised either by cyclisation of acyclic compound or by interconversion among appropriately substituted thiazolidinone derivatives. Different methods for the preparation of 4-thiazolidinones have been described[10–17].



a: benzene; b: thiolactic acid; R′: *m*-phenoxy-phenyl

In continuation of our work on 4-thiazolidinone derivatives[18–20], we have undertaken the synthesis of 4-thiazolidinones of type (**IIa–w**) by the condensation

of *m*-phenoxy benzaldehyde with aryl amines yielding Schiff bases **(Ia–w)** which on further treatment with thiolactic acid gave substituted 4-thiazolidinones. The structures of the synthesized compounds were assigned on the basis of elemental analysis, IR and ^{1}H NMR spectral data. All the compounds were evaluated for antimicrobial screening.

EXPERIMENTAL

All the melting points were determined in an open capillary tube and are uncorrected. The IR spectra were recorded on Perkin-Elmer 237 spectrophotometer. ^{1}H NMR spectra on a Bruker Avance DPX 200 MHz spectrometer with $CDCl_3$ as a solvent using TMS as internal reference (Chemical shift in δ ppm). Purity of the compounds was checked on TLC using silica gel-G.

Preparation of 2-(3′-phenoxy phenyl)-3-(4′-phenoxy phenyl)-5-methyl-4-thiazolidinone (IIr)

A mixture of *m*-phenoxy benzaldehyde (0.01 mol) and *p*-amino diphenyl ether (0.01 mol) was refluxed in dry benzene (50 mL) using Dean-Stark water separator. The reaction mixture was refluxed continuously till theoretical quantity of water separated. It was cooled and thiolactic acid (0.012 mol) was added in it and further refluxed till theoretical quantity of water separated from the reaction mixture. Excess of solvent was distilled off under reduced pressure. The isolated product 2-(3′-phenoxy phenyl)-3-(4′-phenoxy phenyl)-5-methyl-4-thiazolidinone was treated with 10% $NaHCO_3$ solution to remove excess of thiolactic acid. The product was then recrystallised in alcohol.

IR (KBr): 1675 cm^{-1} ν(C=O), 680 cm^{-1} ν(C—S—C thiazolidine ring), 1250 cm^{-1} ν(C—O—C) and 1130 cm^{-1} ν(C—N).

NMR ($CDCl_3$): 6.00 δ (s, 1H, CH—Ar), 4.10 δ (q, 1H, CH—CH_3), 1.70 δ (d, 3H, CH—CH_3) and 6.80 to 7.40 δ (m, 18H, aromatic proton).

Similarly other compounds **(IIa–w)** were also prepared by the above method. All compounds gave satisfactory elemental analysis. The physical and analytical data are recorded in Table-1.

Antimicrobial Activity

The antimicrobial activity of the synthesised compounds was screened against both gram +ve and gram –ve bacteria employing the cup-plate agar diffusion method[21]. The micro-organisms employed were *Staphylococcus aureus, Escherichia coli, Bacillus subtilis, Serratia marcescens, Proteus vulgaris* and *Pseudomonas aeruginosa*. The nutrient agar broth was inoculated aseptically with 0.5 mL of 24 h old subculture of organism in a separate flask at 40–50°C. 25 mL of contents were poured and evenly spread in a petridish (9.0 cm in diameter) and allowed to set for 2 h. The cups (7 mm in diameter) were formed and filled with 0.1 mL (1 mg/mL) solution of sample in DMF.

The plates were incubated at 37°C for 24 h. The control was also maintained with 0.1 mL of DMF in similar manner and the zones of inhibition of the growth were measured in mm (Table-2). Known antibiotics like ampicillin showed a zone

TABLE-1
PHYSICAL AND ANALYTICAL DATA OF COMPOUNDS

Compd. No.	R	m.f.	m.p. (°C)	Elemental anaylsis% Found (Calcd)		
				C	H	N
IIa	phenyl	$C_{22}H_{19}NO_2S$	limpid	73.07 (73.13)	5.13 (5.26)	3.76 (3.88)
IIb	2-chloro phenyl	$C_{22}H_{18}NO_2SCl$	impid	66.60 (66.75)	4.52 (4.55)	3.40 (3.54)
IIc	3-chloro phenyl	$C_{22}H_{18}NO_2SCl$	impid	66.75 (66.75)	4.40 (4.55)	3.38 (3.54)
IId	4-chloro phenyl	$C_{22}H_{18}NO_2SCl$	impid	66.77 (66.75)	4.48 (4.55)	3.51 (3.54)
IIe	2-methyl phenyl	$C_{23}H_{21}NO_2S$	limpid	73.50 (73.60)	5.49 (5.60)	3.71 (3.73)
IIf	3-methyl phenyl	$C_{23}H_{21}NO_2S$	limpid	73.58 (73.60)	5.58 (5.60)	3.62 (3.73)
IIg	4-methyl phenyl	$C_{23}H_{21}NO_2S$	limpid	70.57 (73.60)	5.20 (5.60)	3.51 (3.73)
IIh	2-methoxy phenyl	$C_{23}H_{21}NO_3S$	limpid	70.57 (70.59)	5.20 (5.37)	3.51 (3.58)
IIi	3-methoxy phenyl	$C_{23}H_{21}NO_3S$	limpid	70.61 (70.59)	5.31 (5.37)	3.42 (3.58)
IIj	4-methoxy phenyl	$C_{23}H_{21}NO_3S$	85	70.48 (70.59)	5.28 (5.37)	3.56 (3.58)
IIk	2-ethyl phenyl	$C_{24}H_{23}NO_2S$	limpid	74.04 (74.04)	5.93 (5.91)	3.60 (3.60)
III	4-ethyl phenyl	$C_{24}H_{23}NO_2S$	limpid	73.96 (74.04)	5.90 (5.91)	3.47 (3.60)
IIm	2-ethoxy phenyl	$C_{24}H_{23}NO_3S$	limpid	71.01 (71.11)	5.62 (5.68)	3.52 (3.46)
IIn	4-ethoxy phenyl	$C_{24}H_{23}NO_3S$	limpid	71.08 (71.11)	5.66 (5.68)	3.44 (3.46)
IIo	3-acetamido phenyl	$C_{24}H_{22}N_2O_3S$	limpid	68.80 (68.90)	5.29 (5.26)	6.54 (6.70)
IIp	4-acetamido phenyl	$C_{24}H_{22}N_2O_3S$	185	68.78 (68.90)	5.13 (5.26)	6.66 (6.70)
IIq	2-phenoxy phenyl	$C_{28}H_{23}NO_3S$	81	74.16 (74.17)	5.07 (5.08)	3.03 (3.09)
IIr	4-phenoxy phenyl	$C_{28}H_{23}NO_3S$	115	74.10 (74.17)	5.01 (5.08)	3.08 (3.09)
IIs	2,3-dichloro phenyl	$C_{22}H_{17}NO_2SCl_2$	impid	61.43 (61.40)	4.00 (3.95)	3.28 (3.26)
IIt	2,5-dichloro phenyl	$C_{22}H_{17}NO_2SCl_2$	impid	61.27 (61.40)	3.90 (3.95)	3.15 (3.26)
IIu	4-bromo phenyl	$C_{22}H_{18}NO_2SBr$	limpid	60.04 (60.00)	4.05 (4.09)	3.08 (3.18)
IIv	1-naphthyl	$C_{26}H_{21}NO_2S$	limpid	75.79 (75.91)	5.01 (5.11)	3.29 (3.41)
IIw	benzyl	$C_{23}H_{21}NO_2S$	limpid	73.54 (73.60)	5.52 (5.60)	3.60 (3.73)

of inhibition at 22–26 mm and chloramphenicol at 21–28 mm against various stains of bacteria. Compounds **IIb, IIs** and **IIv** exhibited quite good activity against above microbes (Table-2). Compound **IIf** exhibited good activity against *Bacillus subtilis* and *Serratia marcescens*. The other compounds were moderate active or inactive against these microbes.

TABLE-2
ANTIMICROBIAL ACTIVITY OF COMPOUNDS

Compd. No.	R	Diameter of zone of inhibition (in mm)					
		S. aureus	*E. coli*	*B. subtilis*	*S. marcescens*	*P. vulgaris*	*P. aerugenosa*
IIa	phenyl	—	—	—	—	—	—
IIb	2-chloro phenyl	12	12	9	15	17	18
IIc	3-chloro phenyl	12	10	—	10	—	—
IId	4-chloro phenyl	15	10	—	10	—	—
IIe	2-methyl phenyl	11	10	—	—	—	—
IIf	3-methyl phenyl	—	—	20	27	—	—
IIg	4-methyl phenyl	9	12	—	—	11	8
IIh	2-methoxy phenyl	18	—	12	—	—	—
IIi	3-methoxy phenyl	12	9	—	10	9	9
IIj	4-methoxy phenyl	9	—	10	—	—	—
IIk	2-ethyl phenyl	14	22	—	—	—	8
III	4-ethyl phenyl	13	—	—	—	—	—
IIm	2-ethoxy phenyl	10	—	—	—	—	—
IIn	4-ethoxy phenyl	—	—	—	—	—	—
IIo	3-acetamido phenyl	15	—	—	22	—	—
IIp	4-acetamido phenyl	11	9	—	—	9	10
IIq	2-phenoxy phenyl	13	9	—	—	—	—
IIr	4-phenoxy phenyl	—	10	17	10	—	—
IIs	2,3-dichloro phenyl	16	20	20	20	15	17
IIt	2,5-dichloro phenyl	9	10	—	—	9	—
IIu	4-bromo phenyl	—	9	—	—	—	—
IIv	1-naphthyl	14	13	10	20	22	22
IIw	benzyl	15	—	—	—	—	—

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